Docket No.: 0020-5273PUS1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Design Application of:
Kouji YOSHIKAWA

Application No.: Not Yet Assigned

Confirmation No.:

Filed: July 9, 2004

Art Unit: N/A

For: PROCESS FOR PRODUCTION OF 3,3-DIMETHYL-2-FORMYLCYCLOPROPANECARBOXYLIC ACID DERIVATIVES

Examiner: Not Yet Assigned

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The PTO is requested to use the amended sheets/claims attached hereto (which correspond to Article 19 amendments or to claims attached to the International Preliminary Examination Report (Article 34) during prosecution of the above-identified national phase PCT application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: July 9, 2004

Respectfully submitted,

By _____
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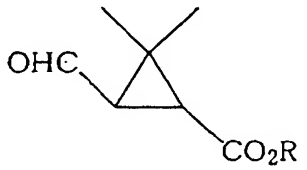
Attachment(s)

alkenyl groups, there has been known, for example, a process in which the 3,3-dimethyl-2-formylcyclopropanecarboxylic acid derivative of formula (2):



(2)

wherein R is as defined above, are reacted with Wittig reagents (see, *e.g.*, J. Labelled Compounds and Radiopharmaceuticals, 13, 561(1977)). The 3,3-dimethyl-2-formylcyclopropanecarboxylic acid derivatives of the above formula (2) become important compounds in the synthesis of the above analogs.

As the processes for the production of the 3,3-dimethyl-2-formylcyclopropanecarboxylic acid derivative of formula (2), there have been known, for example, a process in which the 3,3-dimethyl-2-(2-methyl-1-propenyl)-cyclopropanecarboxylic acid compound of the above formula (1) are oxidized in the presence of an osmium tetroxide catalyst (see, *e.g.*, J. Labelled Compounds and Radiopharmaceuticals, 13, 561(1977)) and a process in which the 3,3-dimethyl-2-(2-methyl-1-propenyl)cyclopropanecarboxylic acid compounds of the above formula (1) are oxidized with ozone (see, *e.g.*, JP-B 46-24695). However, since the former process uses highly toxic osmium tetroxide and the latter process has a tendency to need large-scale equipment, both cannot be said to be production processes suitable on an industrial scale.

Journal of the Chemical Society, Perkin Transactions I, 1980 pages 1711-1717 discloses a process for preparing cis-2,2-formyl-3,3-diemethylcyclopropanecarboxylate by oxidizing a chrysanthemate with sodium metaperiodate in the presence of the catalyst, osmium tetraoxide. However, this process also uses highly toxic osmium tetroxide and cannot be

said to be a process suitable on an industrial scale. EP-A 0 444 708 discloses a process for preparing a ketone or aldehyde compound by oxidizing an olefin compound having a β-lactam structure. JP-A 5-229981 discloses a process for preparing an aromatic acetaldehyde by oxidizing an allyl substituted aromatic compound with sodium periodate in the presence of a ruthenium catalyst and a phase transfer catalyst. JP-A 55-087739 discloses a process for preparing an aromatic aldehyde by oxidizing an α, β unsaturated aromatic compound in the presence of an oxidizing agent and a ruthenium catalyst. However, the oxidization disclosed in these processes are not compared to the above oxidization of the compound of the above formula (1).

Disclosure of Invention

Under these circumstances, the present inventor has intensively studied a process for the production of the 3,3-dimethyl-2-formylcyclopropanecarboxylic acid derivative of the above formula (2) on an industrial scale and has found that the desired 3,3-dimethyl-2-formylcyclopropanecarboxylic

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 663567	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP 02/13576	International filing date *(day/month/year)* 26.12.2002	Priority date *(day/month/year)* 10.01.2002
International Patent Classification (IPC) or both national classification and IPC C07C51/373		
Applicant SUMITOMO CHEMICAL COMPANY, LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.07.2003	03.05.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Delanghe, P Telephone No. +31 70 340-4119

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP 02/13576

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1, 3-23	as originally filed
2	received on 22.03.2004 with letter of 22.03.2004

Claims, Numbers

1-6	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-6
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Documents

Reference is made to the following documents:

D1: Journal of the Chemical Society, Perkin Transactions I; 1980, 1711-1717
D2: EP-A-0444708
D5: Fieser and Fieser, Reagents for Organic Chemistry, 1967, pages 813-814
D6: Fieser and Fieser, Reagents for Organic Chemistry, vol. 5, page 508
D7: Fieser and Fieser, Reagents for Organic Chemistry, vol. 11, pages 462-463

The documents D5-D7 were not cited in the international search report. Copies of the documents are appended hereto.

2. Subject matter

Claims 1-6 define a process for the production of 3,3-dimethyl-2-formylcyclopropanecarboxylic acid and some of its ester derivatives. The process involves the treatment of the 3,3-dimethyl-2-(2-methyl-1-propenyl)cyclopropanecarboxylic acid or an ester derivative thereof with a periodic acid in the presence of a ruthenium catalyst.

3. Novelty

There are no documents in the prior art disclosing the oxidative degradation of 3,3- dimethyl-2-(2-methyl-1-propenyl)cyclopropanecarboxylic acid or some of its ester derivatives to yield 3,3-dimethyl-2-formylcyclopropanecarboxylic acid or some of its ester derivatives, using a periodic acid and a ruthenium compound. Consequently, the subject-matter of claims 1-6 is novel (Art. 33(2) PCT).

4. Inventive step

Document D1, which is considered to represent the most relevant state of the art, discloses a process for the preparation of methyl 3,3-dimethyl-2-formylcyclopropanecarboxylate using a periodic acid and an osmium metal catalyst, from which the subject-matter of the claim 1 differs in that a ruthenium metal catalyst is used instead of osmium. The problem to be solved by the

present invention may therefore be regarded as an oxidative cleavage process, suitable to be used on an industrial scale, starting from an alkene-containing substrate for the preparation of 3,3-dimethyl-2-formylcyclopropanecarboxylic acid or its esters, using a less toxic metal catalyst. The solution proposed in claim 1 of the present application can be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

A less toxic ruthenium metal catalyst is used in the oxidative cleavage reaction of a 3,3-dimethyl-2-(2-methyl-1-propenyl)cyclopropanecarboxylic acid derivative of formula 1 to a 3,3-dimethyl-2-formylcyclopropanecarboxylic acid derivative instead of the more toxic osmium metal catalyst.

In addition, D2 teaches (see examples) a process for the oxidative cleavage, using ruthenium trichloride and periodic acid, of an alkene group to an aldehyde group. However, the combination of the teaching of D1 and D2 is not obvious because in D2 the alkene moiety is directly attached to a betalactam ringstructure and the alkene moiety is disubstituted, whereas in the invention and in D1, the alkene moiety is directly attached to a cyclopropane ringstructure and the alkene moiety is trisubstituted.

Moreover, D5-D7 teaches that the combination of ruthenium metal and periodate is also known to cleave alkenes to give acids and therefore high yields of aldehyde could not have been expected.

The documents of the prior art do not disclose any processes which solve the problem in the same way as the present application. Thus, given the teaching of the prior art, the skilled person would not consider solving the problem in the same way as the present application, and he certainly would not expect the improvement associated with the present application. Therefore, the solution proposed in claim 1 of the present application can be considered as involving an inventive step (Article 33(3) PCT).

Claims 2-6 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty and inventive step.